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Nanoparticle-Based Therapy in Genomics

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Abstract: In the modern era, humankind is making daily progress through industrialization. As various types of diseases are prevailing worldwide, scientists are using many approaches to manage these diseases, such as gene therapy. A nanoparticle (NP)-based approach is an example of a modern method used to address several pathologies. This modern therapeutic approach aims not only at safely transferring the drug of choice to the site of interest in a biological system but also at ensuring the biocompatibility of these NPs. Hence, various coating methodologies are being employed to avoid NP toxicity as well as immunoreactivity. This short review covers the latest approaches and advances in this biomedical field. Among nanomaterials, gold NPs (GNPs) are comprehensively employed as a diagnostic tool for the treatment and management of diseases such as cancer.

Keywords: Cancer, diseases, gene therapy, gold nanoparticles, health, nanoparticles.

INTRODUCTION

Currently, nanotechnology is a rapidly growing field in modern science, and it is in the revolutionary phase of its technological development as an advanced biomedical science [1]. Nanoscience/nanotechnology illustrates that technology and science can connect on the nanoscale level (via nanoparticles (NPs)) to allow for the investigation and regulation of the relationships between biological systems and non-biological (synthetic) materials at the cellular level [2]. Nanotechnology can be employed as a well-organized tool for navigating the most important processes in biological development and biomedical sciences [3, 4]. Within nanotechnology, NPs address the production and association of matter at the level of molecules that are smaller than 1 nm [5]. The size of NPs corresponds to that of most biological structures and molecules; the diameter of fine particles ranges from 100 to 2500 nm, whereas that of ultra-fine particles ranges from 1 to 100 nm. Despite their diminutive structure, NPs can cause a chemical reaction and show activity because of their distinctive crystallographic characteristics, which enhance their surface area and thus increase the extent of their reactivity [6, 7].

NANOPARTICLES IN MEDICINE

Various applications of nanomaterials in medicine are evident [8] and are summarized in (Fig. **1**).

SYNTHESIS OF NANOPARTICLES

Various methods are employed for the synthesis of nanomaterials/NPs using a wide range of materials. Metallic NPs are prepared by the process of emulsifying metals, dendrimers and molten salts. In general, five synthetic methods are mainly used to synthesize metal colloids (Fig. **2**).

For the treatment of various pathological states, such as cancer, asthma, diabetes, allergy and infections, a number of NP-based therapeutics have been produced [9, 10]. For instance, based on investigations related to cancer research, nanotechnology has had a large impact not only on diagnostics but also on the treatment of cancer. Several cancerous cells contain an integral protein known as epidermal growth factor (EGF) receptor (EGFR), which is dispersed on the exterior of plasma membranes, whereas non-cancerous cells have less of this receptor protein. By attaching gold NPs (GNPs) to an antibody against EGFR (anti-EGFR), researchers have been able to attach the NPs to cancer cells [11]. Once the attachment has occurred, the cancer cells demonstrate altered light absorption and scattering spectral profiles compared with normal and/or benign cells [12]. Oncologists are able to use the absorbance and scattered spectra for the identification of cancerous cells in biopsy samples.

LIPOSOMES

Liposomes are spherical soft-matter particles consisting of one (unilamellar) or more (multilamellar) phospholipid bilayer membranes and containing a volume of aqueous medium. Structurally, liposomes look similar to cell membranes and can be used as small containers (capsules) to carry bioactive molecules for various biological applications [13]. Chemically, the charge strength/stability and other surface properties depend on the phospholipid employed for the synthesis of the liposomes. Phosphatidic acid, phosphatidylglycerol, phosphatidylserine, stearylamine, phosphatidylethanolamine and phosphatidylcholine are natural phospholipids that are frequently used for the synthesis of liposomes [14]. Liposomes can be unilamellar (one lipid bilayer), multilamellar (many lipid bilayers) or multivesicular (more than one small liposome enclosing a capsule within a large liposomal structure), depending upon the technique of synthesis and the desired application [15].

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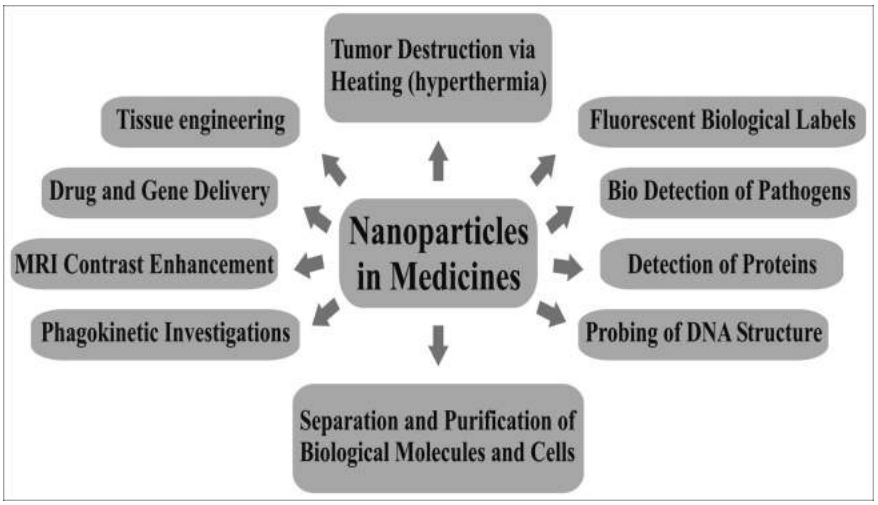

Fig. (1). Applications of nanoparticles in medicine and biology.
MRI = Magnetic Resonance Imaging.

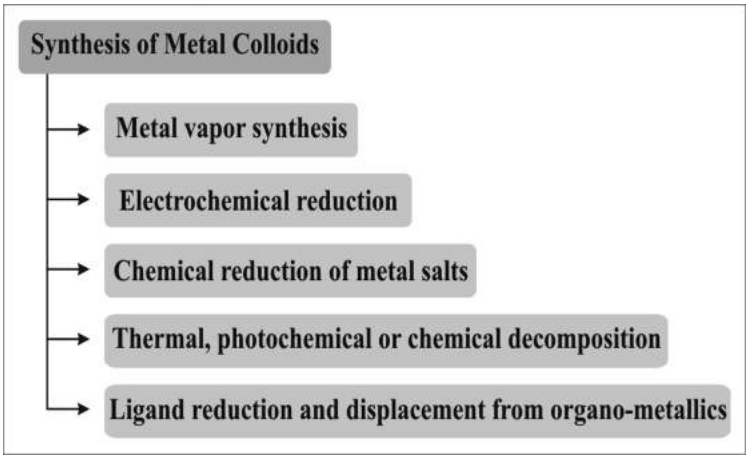

Fig. (2). Methods for the manufacturing of metal colloids (nanoparticles).

For both *in vitro* and *in vivo* delivery, the shell of liposomes can be used to encapsulate or combine numerous, diverse substances. Liposomes have been effectively used for the delivery and release of therapeutic mediators, such as anticancer, antiviral and antibacterial medicines; similarly, nucleic acids, enzymes and hormones have been delivered [16-18]. For the delivery of nucleic acids and drugs, several liposome-based preparations are commercially available [19]. Encapsulation of drug molecules in the interior of liposomes presents numerous advantages, including an increased drug circulation time, shielding from degradation by enzymes and a slow and sustained release of the drug molecules; these are crucial requirements for excellent delivery agents. Moreover, coating with poly(ethylene glycol) (PEG), also called PEGylation, prevents opsonization of NPs, and as a result, PEGylation allows liposomes to escape the immune system and prolongs their circulation in the blood, enabling drug release within the leaky tumor vasculature. The association between nanomedicine and tumors is known as the enhanced permeation and retention (EPR) effect, in which particles enter the leaky tumor vasculature and have a prolonged dwelling time in the biological system because of reduced extracellular drainage.

Functionalized NPs interact exclusively with specific biological macromolecules, such as proteins or DNA. Occasionally, NPs exhibit non-specific interactions with sub-cellular entities, depending on the specific characteristics of the NPs, such as charge and shape. Due to greater penetration facilitated by their shape, carbon nanotubes appear to be more successful than 14 nm carbon black (CB) particles in causing interstitial swelling and epithelioid granuloma in mice [20].

For investigative applications, NPs enable recognition at the molecular level. NPs facilitate the identification of abnormalities, such as pathological markers, precancerous cells and fragments of viruses, that cannot be identified using conventional diagnostic practices. Imaging contrast agents based on NPs have also been shown to improve the sensitivity of magnetic resonance imaging (MRI). The investigation of well-organized and harmless carriers to attain improved drug accessibility at the target site has been an exigent area of exploration. Current research focuses on colloidal NPs (<500 nm), including biodegradable polymeric and liposomal systems as well as bio-conjugation with antitumor drugs. Biocompatible NPs enhance the controlled delivery of drugs to cancerous cells while reducing toxicity toward normal cells. Diverse carriers,

including liposomes, micelles, microcapsules, soluble polymers and lipoproteins, have been used therapeutically to increase the number of drug molecules targeting a specific area (Fig. **3**). For example, anticancer drugs enclosed in liposomes facilitate targeted drug delivery to tumor tissues and avert damage to the normal surrounding tissues. Moreover, anticancer drugs attached to magnetic NPs (MNPs) have been injected into the arterial blood circulation and directed to a tumor by a magnetic field to allow targeted drug release. Research efforts have also been focused on expansion of the utilization of biocompatible and biodegradable NPs (<100 nm) as useful drug delivery systems, particularly for chemotherapy and gene delivery.

TYPES OF NANOPARTICLES THAT ARE USEFUL IN DRUG DELIVERY

A wide variety of NPs are now being used for the targeted delivery of drugs (Table **1**).

GENE THERAPY

NPs are well suited to passing through cellular membranes to achieve gene and/or drug delivery because they are small and compact. It has also been predicted that due to their smaller size, NPs will be less exposed to the phagocytic cells (macrophages and monocytes) involved in the immune response and will show improved infiltration into tissues and cells when used as an *in vivo* treatment. Gene therapy has been anticipated as a prospective approach for curing neurodegenerative disorders, cancers and genetic and infectious diseases, such as hemophilia, cystic fibrosis, tuberculosis, asthma and dystrophies. Therapeutics related to genes are dependent on the use of delivery vectors due to the labile characteristics of the therapeutics and their poor infiltration across the cell membrane as well as into the nuclear location of the target [21]. The world's first gene therapeutic, Gendicine (a p53-based, apoptosis-causing cancer gene therapy), was approved in 2004 in China for the management of cancer in the region of the head and neck [22]. Another example is Rexin-G, which is used in the treatment of numerous neoplastic conditions, including breast cancer, advanced colon cancer and pancreatic cancer. There are also a number of investigations exploring the effectiveness of using small interfering RNAs (siRNAs) as cancer therapies.

The principle of gene therapy is to manipulate the physiology and signal transduction of the biological environment by overexpressing or down-regulating one or a number of genes. The process of down-regulating a gene can be accomplished by the transfer of short antisense oligonucleotides into cells or by the intracellular delivery of recently designed siRNAs. Additionally, a gene of inter-

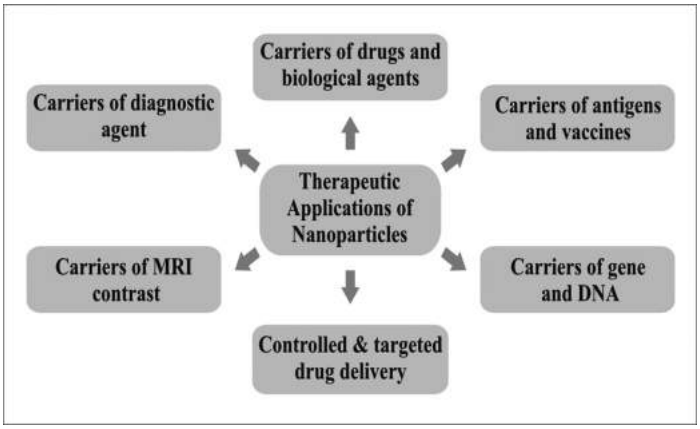

Fig. (3). Therapeutic applications of nanoparticles in the field of biomedical sciences.

Table 1. Various types of nanoparticles that are useful as drug delivery systems.

Nanoparticles	Significance
Carbon nanotubes	Gene and DNA delivery and drug release
Ceramic nanoparticles	Delivery of drugs and biological molecules
Liposomes	Targeted drug delivery
Magnetic nanoparticles	Targeted diagnostics in medicine
Nano films	Systemic or local drug delivery
Nanopores	Release of drug carriers
Nanoshells	Tumor targeting
Polymeric micelles	Controlled and systemic delivery of water-insoluble drugs
Polymeric nanoparticles	Targeted drug delivery
Quantum dots	Targeting and imaging agent (e.g., in MRI)

est can be expressed by translocating plasmid DNA into cells containing the sequence of the gene under the control of a promoter. Vectors are used for attaching and delivering nucleic acids to cells by physical means to transfer genetic material into the nucleus of the cells for gene expression. Among the various methods designed for delivering genes, gene carriers have been comprehensively investigated for the introduction of free nucleic acids (transfection) into mammalian cells. Gene carriers are commonly separated into two major groups (Fig. **4**).

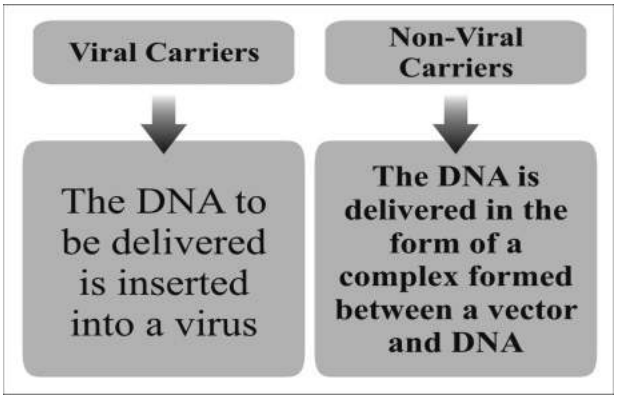

Fig. (4). Two major types of gene carriers.

Viral delivery methodology involves genetically engineered recombinant viruses that transmit remedial genes via their viral capsid, consequently shielding the genes from enzymatic degradation. Viral vectors are effective, but their use is still limited by safety and manufacturing issues. Moreover, the threat of an immune response to the viral particle remains, which does not allow for repetitive *in vivo* administration. Non-viral gene delivery methodologies have a number of advantages over viral methodologies, such as stability, low cost, safety, ease of manufacturing and high flexibility concerning the size of the delivered transgene. These non-viral vectors are less complicated to characterize than viral vectors are, although the *in vivo* expression levels of the genes delivered by non-viral gene delivery methods are lower than those following viral delivery.

(I) Neurotransmitter and Cytokine mRNA Expression Due to Nanoparticle Exposure

In vivo real-time PCR and microdialysis methods have been used to investigate the consequence of the administration of NPs alone on proinflammatory cytokines and neurotransmitters in the mouse olfactory bulb. Compared with control mice, CB-transfused mice had statistically significantly enhanced extracellular glycine and glutamate levels, even though no change in GABA or taurine levels was observed in the olfactory bulb. Immunological parameters, such as IL-1β and TNF-α mRNA expression, were observed to be significantly increased in the olfactory bulb of the CB-instilled mice compared with the controls. The results illustrated that in mice, CB/NPs might transform the extracellular levels of proinflammatory cytokine mRNA expression as well as of amino acid neurotransmitters in a manner that involves interacting with lipoteichoic acid in the olfactory bulb [23].

(II) Dendrimers

Dendrimers can be employed for gene therapy and may represent a substitute for conventional viral vectors. Dendrimers penetrate into cells by endocytosis, and the encapsulated DNA is transported into the nucleus for transcription of the gene of interest. The advantage of dendrimer-based therapy is the dearth of stimulation of the immune response. Dendrimer-based nanomedicines have been used for the treatment of various diseases, including epithelial cancer and other cancers, malaria, and HIV infection [24-26].

NPs have been observed to be fully integrated into biological structures and physiological systems. For instance, biogenic MNPs occur naturally in numerous organisms, ranging from bacteria (unicellular) to protozoa to animals (multicellular) [27]. A biological representation of coated nanomaterials also found in humans is ferritin, which is an iron-containing protein that is approximately 12 nm in diameter and that contains 5 nm- to 7 nm-sized hydrous ferric oxide surrounded by a protective protein covering.

There are numerous approaches for the bio-conjugation of NPs, including attachment to elastin, antigen-antibody interaction, antisense oligonucleotide use, biotin-avidin interaction, and peptide or protein use [28-30]. The distinctive biokinetic behavior of NPs guarantees applications in therapeutic and diagnostic devices and in tools for exploring and understanding structures and molecular processes in living cells. Additionally, due to the particular biokinetic behavior of NPs, involving cellular endocytosis; transcytosis; circulatory, neuronal and lymphatic distribution; and translocation, bio-conjugated NPs are attractive for use in medical applications that may be connected with potential toxicity.

The blood supply of tumors plays an important role in the release of therapeutic agents in tumors. The tumor vasculature differs both morphologically and functionally from the vasculature in normal tissues. Tumor blood vessels are normally larger in size, heterogeneous in distribution and more permeable. The enhanced permeability of the tumor vasculature is believed to be regulated by a variety of mediators, such as bradykinin, nitric oxide, vascular endothelial growth factor (VEGF), matrix metalloproteinases and prostaglandins [31]. Various cellular mechanisms, such as modification of precise enzyme activities or transport mechanisms, including P-glycoprotein (Pgp)-associated multidrug resistance (MDR) and apoptosis regulation, may contribute to the resistance of tumors to therapeutic drugs. MDR is mostly due to the overexpression of the membranous Pgp, which is responsible for releasing a range of usually positively charged xenobiotics from the cell, including certain anticancer drugs. The commonly used anticancer drugs, including tamoxifen, fluorouracil, paclitaxel, cisplatin and doxorubicin, are toxic to both tumor and normal cells; therefore, the effectiveness of chemotherapy is frequently limited by severe side effects [32]. The problems that normally occur among drugs are low bioavailability, insufficient *in vitro* stability (shelf life), poor solubility, short *in vivo* stability (half-life), strong side effects, regulatory hurdles and a lack of large-scale production.

Traditionally, two methods are employed in anticancer drug delivery: 1) affinity targeting and 2) passive targeting. The former method attempts to take advantage of overexpressed tumor-related antigens or receptors to selectively target a drug to a tissue through a chemical interaction with targeting carrier, such as a peptide, antibody fragment or antibody. In contrast, in passive targeting, NPs or macromolecular carriers take advantage of the EPR effect, which is the result of the increased vascular permeability and decreased lymphatic flow associated with tumors, to target a medicine to a tumor [33].

ASSOCIATION CHEMISTRY OF NANOPARTICLES

The chemical associations between modified NPs and biomolecules are principally electrostatic in nature, whereas hydrophilic and hydrophobic contacts are present among organic chains. Negatively charged DNA chains, for example, intermingle with positive amino groups, resulting in the adsorption (loading) of the DNA on modified NPs. This physical association means that the loading of the biological molecule is reliant on the charge density, the modified structure and the chain length. This interaction keeps macromolecules (such as DNA) from being degraded by enzymes in the plasma due to electrostatic repulsion and the steric effect of the modifiers. This feature is particularly significant in gene therapy because nucleic acids are attacked by enzymes in the plasma.

An increasing number of inorganic NPs have been investigated as carriers for the cellular delivery of a variety of drugs, including proteins [34-36]. Modifications depend on the type of NP, which must present definite functional groups on the surface. In this regard, silica NPs are frequently modified with silane species, whereas GNPs can be modified with thiol groups for gene transfection due to the strong chemical attraction between gold and thiol (-SH) groups. It has been observed that when attached to PEG-folic acid (PEGylation), silane-modified MNPs show a 5-fold increase in cellular uptake by breast cancer cells compared with those only attached to PEG [37, 38].

GOLD NANOPARTICLES AND CANCER THERAPY

GNPs have various useful physical and biochemical characteristics, allowing them to be applied as photothermal and contrast agents and radiosensitizers, and they are also being explored as drug carriers. These are promising mediators for cancer therapy as well. GNPs demonstrate exclusive physicochemical characteristics, such as the ability to react with functional groups (thiols and amines) and to facilitate surface modifications and surface plasmon resonance (SPR) in various applications in biomedical sciences [39]. There have been extensive discussions concerning the mechanism of entrance of GNPs into the biological system. Receptor-mediated endocytosis (RME, which is non-specific) is considered as the most likely mechanism [40]. NPs accumulate in their inactive state at the site of cancerous cells, which exhibit leaky and immature vasculature (wider perforations) compared with normal blood vessels, even without the surface modifications of NPs [31], referred to as the EPR effect. EPR facilitates drug release at the site of cancer cells. Moreover, detection of particles and uptake by phagocytic cells have been investigated [41].

Uptake by phagocytic cells (reticuloendothelial system, or RES) can be reduced by PEGylation, which produces a hydration sphere, causing a steric impediment to the attachment of phagocytes [42]. Furthermore, with the help of PEGylation, the circulation time and the EPR effect of particles can be improved. As a result, the drug concentration is enhanced by 10-100-fold at the site of cancer cells compared with the concentration following the use of a drug without NPs [43]. Cancer drug targeting can be improved by attaching cancer-specific detection molecules, such as folic acid, monoclonal antibodies, EGF or transferrin, to NPs [11, 44, 45].

There are two major mechanisms that stabilize GNPs: a) thiols are highly attracted to gold, resulting in a crowded coating layer of thiolated DNA on the surface of the particles, and b) the DNA backbone contains many negative charges due to its phosphate groups, resulting in a strongly negatively charged coating around the NPs that prevents other charged molecules and NPs from approaching.

TOXICITY AND NANOMEDICINES

Because of their increased handling in the hard metal industry, tungsten carbide cobalt (WC-Co) and tungsten carbide (WC) NPs are of significance to industrial health. Previous investigations have revealed an enhanced noxious potential for WC-Co compared with WC or cobalt ions alone. It was determined that WC NPs exerted extremely small effects on the transcriptomics level after exposure for 3 hours and 3 days. In contrast, WC-Co NPs caused statistically significant transcriptional changes comparable to those aggravated by $CoCl_2$. However, $CoCl_2$ exerted even more prominent changes in transcriptional patterns. A gene set enrichment analysis illustrated that the distinguishably expressed genes were associated with targets of numerous transcription factors, carbohydrate metabolism, endocrine pathways and hypoxia responses. The function of the transcription factor hypoxia-inducible factor 1 (HIF1) was highlighted; moreover, the characteristics of downstream actions as well as the role of other transcription factors associated with cobalt toxicity were measured. It was concluded that WC NPs caused limited transcriptional responses, whereas WC-Co NPs were capable of inducing responses comparable to those induced by free cobalt ions, and mainly the stimulation of hypoxia-like effects through interactions with HIF1 in human keratinocytes. However, in contrast to $CoCl_2$, the increased toxicity of WC-Co particles could not be elucidated based on variations in gene transcription [46].

Induction of inflammation, interference with the normal functioning of cells and tissues, biodistribution, biodegradation and biocompatibility are several of the qualities that determine the toxicity of synthetic inorganic NPs and carbon nanostructures and, consequently, the potential degree of their use. Toxicological investigations of GNPs have been contradictory [47]. In any case, certain investigations have revealed cellular toxicity, including enhanced biosynthesis of reactive oxygen species (ROS) and cytokines, necrosis, apoptosis and mitochondrial toxicity [39, 48-54]. For drug delivery, GNPs have been employed as a carrier covalently linked to cetuximab and gemcitabine for active targeting and as a therapeutic, respectively, in pancreatic cancer [49]. The EGFR is overexpressed on pancreatic cancer cells; however, combination therapy (gemcitabine and cetuximab) has been investigated in a phase II trial for pancreatic cancer [55].

Citrate-coated GNPs with controlled dimensions (2-100 nm) and linked to trastuzumab antibodies were prepared for investigation in human SK-BR-3 breast cancer cells [56]. In addition, using 40 nm GNP-HER particles, the HER-2 receptor complex was observed to be internalized into the cytoplasm, with a 40% reduction in surface HER-2, a process that does not occur with trastuzumab binding alone. This effect was accompanied by reduced expression of downstream kinases, including mitogen-activated protein kinase (MAPK) and protein kinase B (Akt), and a two-fold increase in trastuzumab cytotoxicity.

THERMAL THERAPY

Thermal therapy has been employed along with other types of treatments. Radiation is applied from outside the body or endoluminally for the production of heat through radio waves, ultrasound or microwaves [57]. Advancements in the field of nanomedicine suggest the ability to apply metal particles to the management of tumors/cancer. A source of energy that generates non-ionizing radiation, such as a laser, is used for treatment, and the production of heat is observed due to excitation and relaxation of electrons [58]. Moreover, lasers can be distinctively tuned to the SPR of particles, which differs with the composition, size and shape of the NPs [12].

The majority of investigations have employed gold nanoshells, which have a 15 nm gold coating and a 100 nm silica core. These nanoshells have ability to change the resonance peak to the near infrared region (650-950 nm), in which tissue and blood are maximally transmissive [59].

QUANTUM DOTS

Quantum dots (QDs) have shown potential as an innovative fluorescent label for biomolecules. The finest NPs, QDs, have been used as fluorescence imaging probes. The advantages of QD labels are their tremendously high identification accuracy, controllable colors and high photostability. As imaging contrast agents, NPs/QDs circulate in the blood for longer periods of time, with elevated sensitivity and usually fewer side effects. Moreover, QDs allow the synthesis of newly engineered molecular machines that can measure, manipulate and control biological functions in living cells for the treatment of diseases. This type of NP has attracted considerable attention because QDs represent an important advance in synthetic techniques for preparing high-quality NPs. QDs provide a number of advantages over conventional dyes, including a wide range of excitation wavelengths, size-tunable photoluminescence, good chemical stability and a high quantum yield (more than 50%). As contrast agents, they are suitable due to their high excitability and capacity to produce more bright light over long periods of time. These properties make QDs superior to other accessible labeling reagents, such as organic fluorophores and fluorescent proteins, including green fluorescent protein (GFP) [60].

MAGNETIC NANOPARTICLES

Magnetite NPs (Fe_3O_4) offer a variety of potential applications in various fields. They are superparamagnetic (they display magnetic behavior in magnetic fields) and MRI detectable, with precise microfabrication increasing their MRI sensitivities. Additionally, their surfaces may be designed to perform as drug receptors, and their temperatures may be elevated in alternating magnetic fields [61]. Superparamagnetic iron oxide NPs (SPIONs) composed of crystalline iron oxide surrounded by a coating with dextran or a different polymer have been used to fabricate negative contrast in MRI and to detect liver metastasis and/or involvement of the lymph nodes in metastasis. A previous study demonstrated the utilization of nanocomposites of polylactide nanofibers and tetraheptylammonium-capped Fe_3O_4 MNPs in achieving well-organized accumulation of the anticancer drug daunorubicin in targeted cancerous cells. The effect of using appropriate nanomaterials on drug uptake by cancer cells was then studied. The nanocomposites could successfully assist the interaction of daunorubicin with leukemic cells and improve the anticancer agents' permeation of and uptake by the cancerous cells. This phenomenon led to the death of the leukemic cells [62].

NANOPARTICLES AND NEURODEGENERATIVE DISORDERS

Nanotechnology includes modern atomic and molecular techniques capable of arranging atoms and molecules, respectively, into specifically calculated and controlled patterns [63, 64]. Furthermore, with the help of nanotechnology, it is now possible to target therapeutic agents to particular cells, tissues and organs more successfully and with more favorable outcomes. The significance of the medical applications of nanotechnology is manifested in diseases associated with the central nervous system (CNS) [65]. The small size of NPs/nanomedicines allows them to be conjugated to a number of linkers and modifier compounds for use as treatment strategies without considerably affecting their size [66, 67].

Many important properties make NPs attractive for use in biomedicine. Multiple studies have shown the use of NPs as imaging tools [68, 69] and the use of QDs for labeling microtubules [70]. Silica-based NPs are being used in the development of therapeutic approaches for the delivery of drugs and/or genes. Specifically, organically modified silica (ORMOSIL) particles are porous particles that investigations have shown to be less toxic than QDs [71, 72], with greater cell uptake and delivery [66, 73]. These particles have also shown powerful effectiveness in gene transfer in neuronal tissues and brain cells [74, 75]. For success as a therapeutic tool to treat neuronal disease in humans, NPs must efficiently and specifically integrate into living neuronal tissues, without causing any unfavorable effects in neuronal cells. Investigations have demonstrated that ORMOSIL particles satisfy these criteria. Stereotaxic injections of ORMOSIL particles into the brains of mice have been performed and showed no unfavorable toxic effects in the brain tissue [66, 76].

At present, there is no successful management of or cure for several neurodegenerative disorders. The current dilemma with many of the recent therapeutic treatments is that most are designed for dissociating or dissolving aggregates and preventing cell death in neuronal tissues, which is general neuropathology at the end-stage of disease. Several neurodegenerative disorders exhibit similarities in protein accumulation and neuronal degeneration. However, the type of neurons or the number of neurons affected may vary from disease to disease. In particular, in Alzheimer's disease (AD), degenerating cholinergic neuritis is observed, with amyloid plaques containing an amyloid-beta (Aβ) fragment and anomalous accumulations of hyperphosphorylated tau protein in neurofibrillary tangles. Currently available therapies employed in AD address altering the production of Aβ. Amyloid precursor protein (APP) is catalyzed by two secretase enzymes, β and γ secretase, to produce the small Aβ fragments. During disease, there is amplified cleavage, leading to extensive assembly of Aβ. It is believed that soluble Aβ polymerizes to form oligomers, which collapse (fold) into pleated sheet fibrils that are insoluble in nature, producing senile plaques in neuronal cells. Inhibitors of β and γ secretase, which are reduced through APP cleavage, can be employed in therapeutics. Immunizations against the Aβ peptide can be employed as a potential treatment for AD [77]. A DNA vaccine against AD is also being investigated. This approach does not contain Aβ itself, but as an alternative, it uses a piece of APP [78]. Nanotechnology represents a noninvasive technique to access complex systems, such as the CNS, which is not presently practicable by other approaches [79].

CONCLUSION

Maintaining the health of humans in the modern era, in which we have to cope with changes in the environment, represents a large challenge. As we are facing multiple aspects of various diseases, it is necessary to treat diseases with the latest approaches and advances in biomedical sciences; NP-based approaches remain a potential option. Various investigations are being performed regarding the behavior of nanomedicines in the biological system, which are being considered as promising drug therapy, diagnostics and theranostics for future use. Nanomedicines could be helpful for the management of various diseases, such as cancer, neurodegenerative disorders and other disorders. Nanomedicines may also be a crucial tool for personalized medicine.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Declared none.

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